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09/697,875	10/26/2000	Robert H. Kincaid	10002206-1	5404

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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 01/24/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/697,875

Applicant(s)

KINCAID, ROBERT H.

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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FINAL ACTION

1. This action is in response to papers filed 6 November 2002 in Paper No. 14 in which claims 30-34, 36 and 38 were amended and claims 1-29 and 50-84 were canceled. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 5 dated 14 May 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. However, the arguments are addressed as they apply to the instant rejections. New grounds for rejection are discussed.

Claims 30-49 are under prosecution.

Specification

2. The previous objection to the specification is withdrawn in view of the amendments to the Abstract submitted in Paper No. 14.

Nucleic Acid Sequence Rules

3. The paper copy and computer readable copy of the sequence listing filed 18 December 2002 in Paper No. 15 is acknowledged.

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Information Disclosure Statement

4. The references listed on the 1449 received 10 May 2002 and received 1 October 2002 have been reviewed and considered. A copy of the initialed 1449 is enclosed with this action.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 30-41 and 44-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockhart et al (WO 97/27317, published 31 July 1997).

Regarding Claim 30, Lockhart et al disclose a method of making a microarray comprising: providing a control probe in an array pattern of features on a surface of the microarray substrate, the control probe being attached to the surface in the array pattern, the

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control probe being directly or indirectly labeled with a control label that emits a control signal when excited by a light (Fig. 13a "label b"); and providing an oligomer test probe to features, the test probe being attached in the array pattern such that the features comprise a control probe (constant region) and an oligomer test probe (variable region) (page 71, lines 1-8 and Fig. 13a) wherein the control probes enhance detection of the features without interfering with oligomer test probe hybridization i.e. "ligation enhanced signal detection" as illustrated in Fig. 13a provides improved hybridization specificity and additional sequence information (page 70, lines 24-31).

Regarding Claim 31, Lockhart et al disclose the method comprising adding one end of the control probe to the substrate and directly labeling the control probe with a control label (page 71, lines 23-31 and Fig. 13 a). The claims are given the broadest reasonable interpretation consistent with the broad claim language "directly labeling" and specification wherein "directly labeling" is not defined (see page 7, lines 6-14). As illustrated in Fig. 13a, Lockhart et al the control probe (constant region) is attached to the surface of the substrate and the test probe (variable region) is coupled to the 5' end of the control probe. At ligation site B, the "ligatable oligonucleotide" comprising label B is ligated to the 5' end of the test probe thereby directly labeling the control probe because the control probe-test probe-ligatable oligonucleotide, when ligated, constitute a single sequence. Given the broadest reasonable interpretation of the claims, the ligation labeling of Lockhart et al is encompassed by the claimed "directly labeling".

Regarding Claim 32, Lockhart et al disclose the method comprising adding one end of the control probe to the surface of the substrate and indirectly associating the control label to the control probe by hybridization when exposed to a control-specific target material comprising the control label (page 6, lines 13-23, page 71, line 1-page 72, line 31 and Fig. 13a-b).

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Regarding Claim 33, Lockhart et al disclose the method comprising adding one end of the control probe to the surface of the substrate within the feature; directly labeling the control probe with a control label; indirectly labeling the labeled control probe with a control target label by hybridization when exposed to a hybridization mixture comprising a labeled control-specific target material complementary to the control probe and the labeled test target sample comprises the test label (page 71, line 1-page 72, line 31 and Fig. 13a-b).

Regarding Claim 34, Lockhart et al disclose the method comprising adding one end of the control probe to the surface of the substrate; adding the oligomer test probe to each feature and indirectly labeling the control probe with the control and the oligomer test probe with the test label by hybridization when exposed to a hybridization mixture comprising a labeled control-specific target material complementary to the control probe and the labeled test target sample comprises the test label (page 71, line 1-page 72, line 31 and Fig. 13a-b).

Regarding Claim 35, Lockhart et al disclose the method comprising adding the oligomer test probe to each feature of the substrate and directly labeling the test probe with a test label (Fig. 13a, "label b").

Regarding Claim 36, Lockhart et al disclose the method comprising adding an oligomer test probe to each feature of the substrate and indirectly associating a test label with the oligomer test probe by hybridization when exposed to a test target material that comprises the test label (Fig. 13a, "label a").

Regarding Claim 37, Lockhart et al disclose the method wherein the step of providing the control probe comprise the step of adding one end of the control probe to the surface of the substrate and the step of providing the oligomer test probe comprises the step of adding the oligomer test probe to an opposite end of the control probes such that the control probe is a stilt that extends between the oligomer test probe and the surface such that each feature comprises the control stilt and test probe (Fig. 13 a-b).

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Regarding Claim 38, Lockhart et al disclose the method wherein the step of providing the control probe comprise the step of adding one end of the control probe to the surface of the substrate and the step of providing the oligomer test probe comprises the step of adding one end of the test probe to the surface of the substrate such that each feature comprises the control probe and test probe i.e. Lockhart et al the method comprising "adding" the one end to the surface because the control probe (constant region) to which the test probe is attached is on the surface of the substrate (Fig. 13 a-b).

Regarding Claim 39, Lockhart et al disclose the method wherein the step of providing the control probe comprises presynthesizing the control probe and attaching one end to the surface of the substrate within each feature i.e. mechanically coupling (page 47, lines 14-15).

Regarding Claim 40, Lockhart et al disclose the method wherein the step of providing the oligomer test probe comprises presynthesizing the test probe and attaching one end to the surface of the substrate within each feature (page 62, lines 20-23).

Regarding Claim 41, Lockhart et al disclose the method wherein the step of attaching the presynthesized oligomer test probe comprises attaching the presynthesized oligomer to an opposite end of the presynthesized control probe (page 72, lines 23-31 and Fig. 13 a-b).

Regarding Claim 44, Lockhart et al disclose the method wherein the step of providing the control probe comprises synthesizing the control probe *in situ* within each feature (page 47, line 13).

Regarding Claim 45, Lockhart et al disclose the method wherein the step of providing the test probe comprises presynthesizing the test probe and attaching the presynthesized test probe within each feature (Fig. 13 a-b)

Regarding Claim 46, Lockhart et al disclose the method wherein the step of attaching the presynthesized test probe comprises attaching to an unattached end of the *in situ* synthesized control probe (page 62, lines 20-23, page 71, lines 9-28 and Fig. 13 a-b).

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Regarding Claim 47, Lockhart et al disclose the method of Claim 44 wherein the step of providing the oligomer test probe (i.e. variable region) comprises synthesizing the oligomer *in situ* within each feature (page 71, lines 9-14 and Fig. 13a).

Regarding Claim 48, Lockhart et al disclose the method of Claim 47 wherein *in situ* synthesized test probe is synthesized on an unattached end of the *in situ* synthesized control probe (page 71, lines 9-14 and Fig. 13a).

Response to Arguments

8. Applicant states that the instant invention is drawn to a method of making an array comprising providing a control probe in an array pattern of features and separately providing an oligonucleotide test probe to the array features wherein the control probe is associated with a control label such that after hybridization or during scanning and detection of signals, the control probe and the associated control label provide a reference for the location of the features and wherein the positions of the features on the array are known i.e. "detection of the features is enhanced, using the control probes".

It is noted that "separately providing an oligonucleotide test probe to the array features"; "after hybridization and/or during scanning and detection of signals, the control probe and the associated control label provide a reference for the location of the features"; and "wherein the positions of the features on the array are known" are not limitations of the instant claims. It is also noted that Applicant's comment "separately providing an oligonucleotide test probe to the array features" appears to contradict the limitations of Claim 41 wherein the test probe is attached to the opposite end of the control probe. As such, comments regarding the above recitations do not address the pending claims. Applicant's attempt to define the means by which the control probes enhance detection of the features is noted i.e. "the positions of the

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features on the array are known i.e. detection of the features is enhanced, using the control probes". However, Applicant has not pointed to the specification for support of this definition.

Applicant argues that Lockhart are silent regarding making an array with enhanced feature detectability and fail to disclose making the array using control probes with the test probes on the array. Applicant argues that the constant region of Lockhart et al is not a control probe as is known in the art because their constant region is optional and because their constant region is predetermined and has substantially the same sequence for all the probes on the array. In contrast, Applicant states, the instantly claimed control probes are not optional. The argument has been considered but is not found persuasive because while Lockhart et al states that the constant region is optional, the "optionally" statement does not negate the fact that Lockhart et al discloses the method of making a microarray comprising control and test probes as instantly claimed (page 70, line 24-page 71, line 8). Lockhart et al not only discloses the probes as claimed, but also illustrates the probes (Fig. 13a). Therefore, Lockhart et al discloses the claimed probes.

Applicant argues that in Lockhart (page 71, lines 9-14) the sample nucleic acid hybridizes to the variable region and optionally hybridizes to the constant region. Applicant contrasts the instant invention by stating "for the purposes of the present invention, a control probe, as is known in the art, does not interfere with an assay, but instead provides a reference or a standard." The argument has been considered but is not found persuasive because further reading of page 71 reveals that Lockhart specifically teaches that the components of the probe oligonucleotide/ligation reaction system (i.e. constant region, variable region and ligatable oligonucleotide) are combined a variety of ways to increase the stability of the hybrid duplex and/or improve hybridization specificity" (page 71, lines 29-31) both of which enhance detection. As stated above, the fact that Lockhart et al teach that hybridization to the control probe (constant region) is optional does not negate the fact that Lockhart discloses the method of making the array as claimed. Additionally, Applicant's comment regarding the intended use

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of the control probes i.e. "provides a reference or a standard" is not relevant to the instant claims because comments address limitations not claimed. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that Lockhart et al fail to enable the instantly claimed invention because while the instant claims require two probes each being separately provided to the microarray wherein the control probe is not optional, Lockhart et al teach their microarray optionally comprises a constant region (control probe) and do not teach or suggest using their ligation system for enhanced feature position detection. The argument has been considered but is not found persuasive for two reasons. First, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., separately providing the control and test probes to the microarray and enhanced feature position detection) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Second, in response to applicant's argument that the instantly claimed control probes are used to detect feature position, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Regarding Claim 31, Applicant argues that Lockhart et al do not teach attaching one end of a control probe to the surface of the substrate and directly labeling the control probe as instantly claimed. The argument has been considered but is not found persuasive because as

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illustrated in Fig. 13a, Lockhart et al teach the control probe (constant region) is attached to the surface of the substrate and the test probe (variable region) is coupled to the 5' end of the control probe. At ligation site B, the "ligatable oligonucleotide" comprising label B is ligated to the 5' end of the test probe thereby directly labeling the control probe because the control probe-test probe-ligatable oligonucleotide, when ligated, constitute a single sequence. Given the broadest reasonable interpretation of the claims, the ligation labeling of Lockhart et al is encompassed by the claimed "directly labeling".

Applicant comments that in the instant invention "a control probe does not hybridize with the target nucleic acid sample". However, this comment addresses limitations not in the claims and therefore is irrelevant to the claims and arguments.

Applicant acknowledges the examiner's stated, "the claims are given their broadest reasonable interpretation consistent with the specification" and points to the specification (pages 6 and 17) for a definition of the instantly claimed control probe. Applicant further states that "the definition does not go beyond that which is consistent with the definition...in the art," and as such, the instantly claimed control probe is not the same or analogous to the constant region of Lockhart. The specification defines the control probe as "probes of a specific, known sequence of nucleic acids of known quantity that do not interfere with a hybridization assay of a target sample. In contrast to conventional use of control probes, for the present invention, the control probe does not take up valuable real estate....but instead is populated on each feature of the microarray along with a respective oligomer test probe." (page 6, lines 1-7). Applicant's arguments and comments have been considered but are not found persuasive because the constant region of Lockhart have a specific, known sequence of nucleic acids of known quantity and do not interfere with a hybridization assay of a target sample (page 71, lines 6-8 and Fig. 13a) as described in the specification. However, Applicant is reminded that while the claims are read in light of the specification, limitation from the specification are not read into the claim. Applicant further argues that in contrast to the instant invention,

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Lockhart uses control probes in addition to a ligation reaction system to derive their probes. The argument has been considered but is not found persuasive because the open claim language "comprising" encompasses additional components and or method steps of Lockhart.

Regarding Claims 32-34, Applicant reiterates the arguments presented for Claims 30 and 31 and further argues that Lockhart does not disclose indirectly labeling the control probe with a control label via hybridization with control-specific material comprising a label. The argument has been considered but is not found persuasive because the constant region hybridized to its complement meets the limitations of the claim 32 (page 71, lines 15-23).

Regarding Claims 35-36, Applicant relies on the arguments presented for Claims 30 and 31 and argues that for those reasons, Lockhart does not disclose the limitations of claims 35-36. The arguments are not considered persuasive as stated above regarding claims 30-31.

Regarding Claim 37-38 Applicant argues that Lockhart do not teach or suggest adding one end of a control probe to the substrate and separately adding a test probe to the opposite end of the control probe. The argument has been considered but is not found persuasive because Lockhart clearly illustrates the limitations of Claim 37 i.e. the control probe (constant region) is added to the substrate and the test probe (variable region) is added to the opposite end of the control probe i.e. the constant region is prepared in a separate procedure and coupled to the array (page lines 13-17 and Fig. 13a). Applicant further argues that the limitations of Claim 38 differ from Claim 37 in that Claim 38 requires the test probe be attached at one end to the substrate surface. The claim is broadly drawn to adding one end of the test probe to the surface. It is noted that the claims are limited to a specific means of attachment e.g. attaching the terminal nucleotide of the test probe to a functional group on the surface of the substrate. Lockhart teaches adding one end of the oligomer test probe to the surface of the substrate via adding the test probe to the constant region. As such, Lockhart disclose the limitations of Claim 38.

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Regarding Claim 39, Applicant argues that Lockhart teach control probes on page 47 which differ from their constant region and which are the same as conventional control probes. As such, Applicant argues, Lockhart teaches away from the instant invention. The argument has been considered but is not found persuasive because as stated above, the constant region of Lockhart meets the limitations of the control probes as claimed and as defined in the specification. The fact that Lockhart teaches additional and different control probes does not negate the fact that they clearly disclose the control probes as claimed.

Regarding Claim 40-41, Applicant relies on the arguments presented for Claims 30 and 31 and argues that for those reasons, Lockhart does not disclose the limitations of claims 40-41. The arguments are not considered persuasive for the reasons stated above regarding claims 30-31.

Regarding Claim 44-48, Applicant relies on the arguments presented for Claims 39 and 30 and argues that for those reasons, Lockhart does not disclose the limitations of claims 35-36. The arguments are not considered persuasive for the reasons stated above regarding claims 39 and 30.

9. Claims 30-36, 38-40, 42, 44 and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claim 30, Gentalen et al disclose a method of making a microarray comprising: providing a control probe in an array pattern of features on a surface of a substrate; and providing an oligomer test probe to each feature such that each feature

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comprising a control probe and a test probe i.e. common probe and variable probe (Column 14, line 59-Column 15, line 4) wherein the control probe is associated with a control label that emits a control signal when excited by light (Column 11, lines 1-11).

Regarding Claim 31, Gentalen et al disclose the method comprising adding one end of the control probe to the substrate and directly labeling the control probe with a control label (Column 11, lines 1-11). The claims are given the broadest reasonable interpretation consistent with the broad claim language "directly labeling" and specification wherein "directly labeling" is not defined (see page 7, lines 6-14). Given the broadest reasonable interpretation of the claims, the labeling of Gentalen et al is encompassed by the claimed "directly labeling".

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

Regarding Claim 32, Gentalen et al disclose the method comprising adding one end of the control probe to the surface of the substrate (Column 11, lines 46-48) and indirectly associating the control label to the control probe by hybridization when exposed to a control-specific target material comprising the control label (Column 11, lines 1-11).

Regarding Claim 33, Gentalen et al disclose the method comprising adding one end of the control probe to the surface of the substrate (Column 11, lines 46-48); directly labeling the control probe with a control label (Column 11, lines 1-11); indirectly associating a control label to the control probe by hybridization when exposed to a hybridization mixture comprising a labeled control-specific target material complementary to the control probe and the labeled test target sample comprises the test label (Column 11, lines 1-11).

Regarding Claim 34, Gentalen et al disclose the method comprising adding one end of the control probe to the surface of the substrate (Column 11, lines 46-48); adding the oligomer

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test probe to each feature and indirectly associating the control label to the control probe and test label to the test probe by hybridization when exposed to a hybridization mixture comprising a labeled control-specific target material complementary to the control probe and the labeled test target sample comprises the test label (Column 11, lines 1-11).

Regarding Claim 35, Gentalen et al disclose the method comprising adding the oligomer test probe to each feature of the substrate and directly labeling the test probe with a test label (Column 11, lines 1-11). The claims are given the broadest reasonable interpretation consistent with the broad claim language "directly labeling" and specification wherein "directly labeling" is not defined (see page 7, lines 6-14). Given the broadest reasonable interpretation of the claims, the labeling of Gentalen et al is encompassed by the claimed "directly labeling".

Regarding Claim 36, Gentalen et al disclose the method comprising adding an oligomer test probe to each feature of the substrate and indirectly associating a test label with the oligomer test probe by hybridization when exposed to a test target material that comprises the test label (Column 11, lines 1-11).

Regarding Claim 38, Gentalen et al disclose the method wherein the step of providing the control probe comprises the step of adding one end of the control probe to the surface of the substrate; and the step of providing the test probe comprises adding one end of the oligomer test probe to the surface of the substrate at each location such that each feature comprises the control probe and the oligomer test probe (Column 14, line 59-Column 15, line 4).

Regarding Claim 39, Gentalen et al disclose the method wherein the step of providing the control probe comprises presynthesizing the control probe and attaching one end to the surface of the substrate within each feature (Column 11, lines 46-48).

Regarding Claim 40, Gentalen et al disclose the method wherein the step of providing the oligomer test probe comprises presynthesizing the test probe and attaching one end to the surface of the substrate within each feature (Column 11, lines 46-48).

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Regarding Claim 42, Gentalen et al disclose the method wherein the step of providing the oligomer test probe comprises synthesizing the test probe *in situ* within each feature (Column 11, lines 48-61).

Regarding Claim 44, Gentalen et al disclose the method wherein the step of providing the control probe comprises synthesizing the control probe *in situ* within each feature (Column 11, lines 48-61).

Regarding Claim 47, Gentalen et al disclose the method of Claim 44 wherein the step of providing the oligomer test probe comprises synthesizing the test probe *in situ* within each feature (Column 11, lines 48-61).

Response to Arguments

10. Applicant argues that the common probe of Gentalen et al is not the same as a control probe known in the art and as instantly claimed. Applicant points to the specification (pages 6 and 17) for a definition of the instantly claimed control probe and states that “a control probe is not and does not functions as a test probe and therefore does not hybridize with test target sample”. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a control probe does not function as a test probe and does not hybridize with a test sample) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The specification defines the control probe as “probes of a specific, known sequence of nucleic acids of known quantity that do not interfere with a hybridization assay of a target sample. In contrast to conventional use of control probes, for the present invention, the control probe does not take up valuable real estate....but

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instead is populated on each feature of the microarray along with a respective oligomer test probe.” (page 6, lines 1-7). While limitations from the specification are not read into the claims, the common probes of Gentalen have a specific, known sequence of nucleic acids of known quantity and do not interfere with a hybridization assay of a target sample (Column 3, lines 62-Column 4, line 5; Column 5, lines 14-26 and Fig. 2). As such, Gentalen disclose the control probes as described in the specification.

Applicant further argues that Gentalen are silent regarding using the common probe for enhancing feature detection. In response to applicant's argument that Gentalen are silent regarding enhanced feature detection, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Applicant argues that Gentalen do not disclose the common probes are associated with a control label because they actually teach that labels are incorporated into the test target sample. Applicant further argues that the control samples of Gentalen teach away from the instantly claimed control probes. The arguments have been considered but are not found persuasive. Claim 30 is drawn to a control probe being directly or indirectly labeled with a control label. The control (common) probes of Gentalen are indirectly labeled by hybridization with a labeled target (Column 11, lines 1-11). The specification defines “indirectly labeled” as associated with complementary control-specific target material (page 7, lines 5-16). As such the control probes being labeled by hybridization meet the limitations of the instantly claimed indirectly labeled probes.

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Applicant argues that in contrast to the method of Gentalen, the signal emitted by the control label of the instant invention provides a reference signal that is detected independently of signals emitted from the oligomer test probes and the control probe provides enhanced feature position detection such that reliance of signal intensity and probe placement is reduced. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., independent signal detection and feature position detection) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that both the common probe and the variable probe of Gentalen are designed to both hybridize to the test target sample for purposes of determining target sequence which is different from Applicant's invention. The argument has been considered but is not found persuasive because the intended use of the claimed method does not result in a manipulative or structural difference from the method of Gentalen or microarray product. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Applicant argues that Gentalen fail to enable the instant invention because they do not disclose every element of the claimed invention. The argument has been considered but is not found persuasive for all of the reasons stated above.

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Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 42, 43 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al (WO 97/27317, published 31 July 1997).

Regarding Claims 42, 43 and 49, Lockhart et al teach a method of making a microarray comprising: providing a control probe in an array pattern of features on a surface of a substrate; and providing an oligomer test probe to each feature such that each feature comprising a control probe and a test probe i.e. constant region and variable region (page 71, lines 1-8 and Fig. 13a) wherein the control probe is associated with a control label that emits a control signal when excited by a light (Fig. 13a "label b") wherein the step of providing the control probe comprises presynthesizing the control probe and attaching one end to the surface of the substrate within each feature (page 47, lines 14-15) and they teach *in situ* synthesis of probes on the array using well known techniques (page 62, lines 19-31) e.g. a fully synthesized portion of the probe is attached to the support followed by *in situ* synthesis of the remaining portion of the probe (page 65, lines 24-29) which clearly suggests attaching a presynthesized control portion of the probe and synthesizing *in situ* the test portion of the probe, but they do not specifically teach that the presynthesized control probe is attached on the surface and the test probe is synthesized *in situ* at the feature. Because *in situ* synthesis is time consuming and costly (see Lockhart et al, page 59, lines 18-28) and because the control probes on the array consist of the same constant domain, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe synthesis of Lockhart et al by simply attaching presynthesized control probes to all features of the array as

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they suggest (page 65, lines 24-29) and thereafter synthesizing test probes of differing sequence on the opposite end of the control probe. One skilled in the art would have been motivated to apply the suggested synthesis of Lockhart et al to their probes thereby saving the time and labor costs of *in situ* synthesis for the control portion of their probes and hence for the obvious benefits of economy of time and labor.

Response to Arguments

13. Applicant refers back to the arguments regarding Claim 30 and concludes that Lockhart teaches away from the instant invention. The arguments regarding the rejection of Claim 30 and implied "teaching away" have been thoroughly reviewed and discussed above.

Applicant further argues that the examiner improperly relied on hindsight reconstruction to make the above rejection. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

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14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
January 22, 2003